

1 UNITED STATES COURT OF APPEALS  
2 FOR THE SECOND CIRCUIT  
3  
4

5 August Term 2004  
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7 (Argued: July 11, 2005 Decided: September 16, 2005)  
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9 Docket No. 04-6674-cv  
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14 ANNE RUGGIERO, Individually and as Representative of the  
15 Estate of Albert Ruggiero,  
16

17 Plaintiff-Appellant,  
18

19 -v.-  
20

21 WARNER-LAMBERT COMPANY and PARKE  
22 DAVIS,  
23

24 Defendants-Appellees.  
25 -----  
26  
27

28 Before: JACOBS and B.D. PARKER, Circuit Judges, and HURD,  
29 District Judge.  
30

31 Plaintiff Anne M. Ruggiero appeals from a judgment of  
32 the United States District Court for the Southern District  
33 of New York (Kaplan, J.), dismissing her complaint on a  
34 motion for summary judgment. Ruggiero argues that the  
35 district court erred in: [i] dismissing her claim on a  
36 ground that was first raised in Defendants' summary-

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\* The Honorable David N. Hurd of the United States District  
Court for the Northern District of New York, sitting by  
designation.

1 judgment reply papers, and that was a subject of ongoing  
2 consolidated proceedings in the multi-district litigation  
3 ("MDL") of which Ruggiero's individual case was a part;  
4 and [iii] holding inadmissible medical expert evidence that  
5 her husband's cirrhosis and death was attributable to a  
6 drug manufactured and sold by Defendants.

7 **AFFIRMED.**

8 RONALD R. BENJAMIN, Law Office  
9 of Ronald R. Benjamin,  
10 Binghamton, NY, for Appellant.

11  
12 DAVID KLINGSBERG, Kaye Scholer  
13 LLP, New York, NY (BERT L.  
14 SLONIM and STEVEN GLICKSTEIN,  
15 on the brief), for Appellees.  
16

17  
18 DENNIS JACOBS, Circuit Judge:

19 Plaintiff Anne Ruggiero appeals from a judgment  
20 entered by the United States District Court for the  
21 Southern District of New York (Kaplan, J.), dismissing on  
22 summary judgment a complaint alleging that her husband's  
23 cirrhosis and death were caused by Rezulin, a diabetes  
24 medication manufactured and sold by defendants Warner-  
25 Lambert Co. and Parke Davis ("Defendants"). The ground  
26 for dismissal was that Ruggiero failed to produce  
27 sufficient evidence that Rezulin was capable of causing or

1     exacerbating cirrhosis (so-called "general" causation).  
2     On appeal, Ruggiero argues principally that [i] the ruling  
3     on general causation was error because that issue was  
4     first raised in Defendants' summary-judgment reply papers,  
5     and is a subject of on-going consolidated proceedings in  
6     the multi-district litigation ("MDL") of which Ruggiero's  
7     case is part; and [ii] medical expert evidence attributing  
8     Mr. Ruggiero's cirrhosis and death to Rezulin was  
9     erroneously ruled inadmissible. For the following  
10    reasons, we affirm.

#### 12                               **BACKGROUND**

13           Albert Ruggiero was diagnosed with Type-II diabetes  
14    in 1982, and in May 1997, he began taking Rezulin, a  
15    diabetes medication manufactured and sold by Defendants.  
16    His death on August 24, 1998 was attributed to liver  
17    failure caused by cirrhosis. On March 21, 2000,  
18    Defendants halted distribution of Rezulin at the request  
19    of the Food and Drug Administration, in light of concerns  
20    that the drug caused increased liver toxicity.

21           Anne Ruggiero commenced this product-liability  
22    action, claiming that Rezulin caused Albert's cirrhosis.

1 The case was added to the "[m]ore than one thousand"  
2 Rezulin-related cases consolidated for pretrial  
3 proceedings in the Southern District of New York, before  
4 Judge Kaplan. In re Rezulin Prods. Liab. Litig. (MDL No.  
5 1348), 223 F.R.D. 109, 111 (S.D.N.Y. 2004). Defendants  
6 subsequently moved for summary judgment in Ruggiero's  
7 individual case.

8 The district court granted summary judgment, holding  
9 that Ruggiero produced insufficient evidence of "general"  
10 causation, i.e., evidence that Rezulin is capable of  
11 causing or exacerbating cirrhosis of the liver.<sup>1</sup>  
12 Specifically, the court ruled that the sole evidence of  
13 general causation submitted by Ruggiero--the expert  
14 opinion of Dr. Douglas T. Dietrich--was inadmissible (as  
15 to that issue) under Fed R. Evid. 702 ("Testimony by  
16 Experts") and Daubert v. Merrell Dow Pharmaceuticals, 509  
17 U.S. 579 (1993). The court reasoned that "Dr. Dietrich  
18 was unable to point to any studies or, for that matter,

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<sup>1</sup> General causation bears on whether the type of injury at issue can be caused or exacerbated by the defendant's product. "Specific" causation bears on whether, in the particular instance, the injury actually was caused or exacerbated by the defendant's product. See Amorgianos v. Nat'l R.R. Passenger Corp., 303 F.3d 256, 268 (2d Cir. 2002).

1 anything else that suggested that cirrhosis could be  
2 caused or exacerbated by Rezulin." Dr. Dietrich's opinion  
3 rested on a review of Albert's medical records and a  
4 "differential diagnosis," i.e., a patient-specific process  
5 of ruling out potential causes of an illness as unlikely,  
6 until one cause remains.<sup>2</sup> The court concluded that this  
7 approach did not provide a reliable basis for Dr.  
8 Dietrich's opinion that Rezulin is capable of causing or  
9 exacerbating cirrhosis.

#### 11 DISCUSSION

12 We review the grant of summary judgment de novo. See  
13 Anthony v. City of New York, 339 F.3d 129, 134 (2d Cir.  
14 2003). A ruling as to the admissibility of expert  
15 evidence is reviewed for abuse of discretion. See Gen.  
16 Elec. Co. v. Joiner, 522 U.S. 136, 142-43 (1997) ("On a  
17 motion for summary judgment . . . the question of  
18 admissibility of expert testimony . . . is reviewable  
19 under the abuse-of-discretion standard.").

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<sup>2</sup> The district court assumed for the purpose of analysis that Dietrich relied on a differential diagnosis but noted that "it was not really clear" that he did so.

1 I

2 As a threshold matter, Ruggiero claims that the  
3 district court should not have reached the issue of  
4 general causation.

5 First, she argues that the issue was first raised in  
6 Defendants' summary-judgment reply papers. See, e.g.,  
7 Playboy Enters., Inc. v. Dumas, 960 F Supp. 710, 720 n.7  
8 (S.D.N.Y. 1997) ("Arguments made for the first time in a  
9 reply brief need not be considered by a court.").

10 Assuming that is so, the district court had discretion to  
11 consider it. See Bayway Ref. v. Oxygenated Mktg. &  
12 Trading, 215 F.3d 219, 226 (2d Cir. 2000) (reviewing for  
13 abuse of discretion district court's decision to rely on  
14 evidence submitted with moving party's reply papers).

15 Defendants' moving papers did not argue expressly in  
16 terms of general causation. However [i] the motion was  
17 cast in terms of the broader and subsuming argument that  
18 Ruggiero could not "establish the essential element of  
19 causation"; [ii] a declaration appended to the moving  
20 papers noted that "[t]here are no scientific studies in  
21 the medical literature that conclude Rezulin can cause  
22 cirrhosis"; and [iii] Ruggiero's opposition papers cited

1 as a genuine issue of material fact "[w]hether or not  
2 there are scientific studies in the medical literature  
3 that conclude Rezulin can cause liver failure such as  
4 caused decedent Albert Ruggiero's death." Under the  
5 circumstances, Ruggiero cannot claim that she was blind-  
6 sided by Defendants' reliance on general causation or that  
7 she was prejudiced by the district court's consideration  
8 of that issue.<sup>3</sup> In any event, it is hard for Ruggiero to  
9 claim unfair prejudice now, because she could have claimed  
10 surprise in the district court and sought to file a  
11 responsive sur-reply.<sup>4</sup>

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<sup>3</sup> See, e.g., Bayway, 215 F.3d at 227 (district court properly relied on evidence submitted with moving party's reply, where, inter alia, record showed that opposing party knew such evidence could refute its claim but "chose not to introduce any evidence" of its own); Cifarelli v. Village of Babylon, 93 F.3d 47, 53 (2d Cir. 1996) (district court properly relied on evidence submitted with defendants' summary-judgment reply, where record showed that plaintiff "was fully aware prior to the defendants' reply of" the issue to which evidence pertained); Bridgeway Corp. v. Citibank, 201 F.3d 134, 140 (2d Cir. 2000) (district court's sua sponte grant of summary judgment neither surprised nor prejudiced losing party where, inter alia, party had previously claimed that it had introduced sufficient evidence concerning the very issue on which the court based its decision).

<sup>4</sup> See, e.g., Bayway, 215 F.3d at 227 (district court properly considered evidence submitted with plaintiff's reply brief where, inter alia, defendant "did not move the district court for leave to file a sur-reply to respond"); Bridgeway Corp. v. Citibank, 201 F.3d 134, 140 (2d Cir.

1           Second, Ruggiero argues that the district court  
2     should not have considered the issue of general causation  
3     because that issue [i] is being litigated by the  
4     "Plaintiffs Executive Committee" in the consolidated MDL  
5     proceedings and [ii] implicates the law-of-the-case  
6     doctrine by reason of a previous contrary decision in  
7     those consolidated proceedings (or somewhere else). Even  
8     assuming that the law-of-the-case doctrine would apply,  
9     Ruggiero's brief directs us to no such contrary ruling.

10           In any event, we decline to consider the merits of  
11     this argument because Ruggiero failed to present it to the  
12     district court. Id. We have discretion to consider  
13     issues that a party failed to raise in the district court,  
14     see Booking v. Gen. Star Mgmt. Co., 254 F.3d 414, 418-19  
15     (2d Cir. 2001), but we decline to do so here. For the  
16     reasons stated above, there is no good excuse for  
17     Ruggiero's failure to bring this complaint to the district

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2000) (plaintiff was not prejudiced by district court's sua  
sponte grant of summary judgment where, inter alia,  
plaintiff "did not, before the district court, raise any  
objections based on lack of notice. Nor did it subsequently  
seek to introduce additional evidence that might have  
convinced the district court to change its position."); cf.  
Gwozdzensky v. Magten Asset Mgmt. Corp., 106 F.3d 469, 472  
(2d Cir. 1997) ("[A]bsent manifest injustice or a showing of  
extraordinary need, we will not decide an issue on appeal  
not first presented to the district court.").



1 court's attention; and we are most hesitant to consider it  
2 in the first instance, given the unmatched expertise Judge  
3 Kaplan has acquired while presiding over the Rezulin MDL  
4 over the past five years.

## 6 II

7 The district court granted summary judgment to  
8 Defendants on the ground that Ruggiero submitted no  
9 admissible evidence to show, as a matter of general  
10 causation, that Rezulin can cause or exacerbate cirrhosis  
11 of the liver. Her only submission arguably on point was  
12 the expert opinion of Dr. Dietrich, who concluded with  
13 reasonable medical certainty that "Albert Ruggiero's liver  
14 disease was caused by his taking Rezulin." The district  
15 court ruled it inadmissible under the standards set out in  
16 Fed. R. Evid. 702 and Daubert.

17 Rule 702 states:

18 If scientific, technical, or other specialized  
19 knowledge will assist the trier of fact to  
20 understand the evidence or to determine a fact in  
21 issue, a witness qualified as an expert by  
22 knowledge, skill, experience, training, or  
23 education, may testify thereto in the form of an  
24 opinion or otherwise, if (1) the testimony is  
25 based upon sufficient facts or data, (2) the  
26 testimony is the product of reliable principles  
27 and methods, and (3) the witness has applied the  
28 principles and methods reliably to the facts of

1           the case.

2   As the Supreme Court explained in Daubert, Rule 702

3   requires the district court to ensure that "any and all

4   scientific testimony or evidence admitted is not only

5   relevant, but reliable." 509 U.S. at 589. As to

6   reliability, "Daubert enumerated a list of factors that,

7   while not constituting a 'definitive checklist or test,' a

8   district court might consider . . . : whether a theory or

9   technique has been and could be tested, whether it had

10   been subjected to peer review, what its error rate was,

11   and whether scientific standards existed to govern the

12   theory or technique's application or operation." Nimely

13   v. City of New York, 414 F.3d 381, 397 (2d Cir. 2005)

14   (quoting Daubert, 509 U.S. at 593-94). "[W]hen an expert

15   opinion is based on data, a methodology, or studies that

16   are simply inadequate to support the conclusions reached,

17   Daubert and Rule 702 mandate the exclusion of that

18   unreliable opinion testimony." Amorgianos v. Nat'l R.R.

19   Passenger Corp., 303 F.3d 256, 266 (2d Cir. 2002).

20       A district court's decision as to how the reliability

21   of expert testimony should be determined, as well as the

22   ultimate decision as to whether that testimony is

23   reliable, are reviewed for abuse of discretion. See Kumho

1 Tire Co. v. Carmichael, 526 U.S. 137, 152 (1999); see also  
2 Joiner, 522 U.S. at 142-43 (abuse-of-discretion standard  
3 persists at summary judgment stage).

4 Judge Kaplan applied the Daubert factors and  
5 concluded that there was no reliable basis for Dr.  
6 Dietrich's opinion that Rezulin could cause or exacerbate  
7 cirrhosis of the liver: "Dr. Dietrich was unable to point  
8 to any studies or, for that matter, anything else that  
9 suggested that cirrhosis could be caused or exacerbated by  
10 Rezulin." The judge further concluded that insofar as Dr.  
11 Dietrich's opinion relied on a differential diagnosis,  
12 that technique was insufficiently reliable to support the  
13 opinion as to general causation (though it might suffice  
14 to support an opinion that a drug shown to be capable of  
15 causing the condition likely did so in a particular case).

16 We see no error. A differential diagnosis is "a  
17 patient-specific process of elimination that medical  
18 practitioners use to identify the 'most likely' cause of a  
19 set of signs and symptoms from a list of possible causes."  
20 Hall v. Baxter Healthcare Corp., 947 F. Supp. 1387, 1413  
21 (D. Or. 1996); Hines v. Consol. Rail Corp., 926 F.2d 262,  
22 270 n.6 (3d Cir. 1991) (defining "differential diagnosis"  
23 as a "process whereby medical doctors experienced in

1 diagnostic techniques provide testimony countering other  
2 possible causes . . . of the injuries at issue"). As the  
3 district court observed, this method does not  
4 (necessarily) support an opinion on general causation,  
5 because, like any process of elimination, it assumes that  
6 "the final, suspected 'cause' remaining after this process  
7 of elimination must actually be capable of causing the  
8 injury." Cavallo v. Star Enter., 892 F. Supp. 756, 771  
9 (E.D. Va. 1995), aff'd on this ground, rev'd on other  
10 grounds, 100 F.3d 1150 (4th Cir. 1996); Hall, 947 F. Supp.  
11 at 1413 (noting that a differential diagnosis "assumes  
12 that general causation has been proven for the list of  
13 possible causes it eliminates"). Where an expert employs  
14 differential diagnosis to "'rule out' other potential  
15 causes" for the injury at issue, he must also "'rule in'  
16 the suspected cause," and do so using "scientifically  
17 valid methodology." Id. Here, Dr. Dietrich may have used  
18 a differential diagnosis to rule out competing causes of  
19 cirrhosis without establishing that Rezulin is among them.

20 We cannot say that a differential diagnosis may never  
21 provide a sufficient basis for an opinion as to general  
22 causation. There may be instances where, because of the  
23 rigor of differential diagnosis performed, the expert's

1 training and experience, the type of illness or injury at  
2 issue, or some other case-specific circumstance, a  
3 differential diagnosis is sufficient to support an  
4 expert's opinion in support of both general and specific  
5 causation. Cf. McCulloch v. H.B. Fuller Co., 61 F.3d  
6 1038, 1043-44 (2d Cir. 1995) (district court did not abuse  
7 discretion in ruling that opinion on causation was  
8 admissible, where opinion was based on care and treatment  
9 of plaintiff, medical history, pathological studies,  
10 product's safety data sheet, reference to scientific and  
11 medical treatises, expert's training and experience, as  
12 well as differential diagnosis). The district judge has  
13 broad discretion in determining whether in a given case a  
14 differential diagnosis is enough by itself to support such  
15 an opinion.<sup>5</sup>

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<sup>5</sup> On this score, the district court indicated that even if a differential diagnosis could be probative of general causation in an appropriate case, it was not so here:

It is not at all clear . . . that a district court lacks discretion to conclude in an individual case that an expert's opinion as to general causation based on an unreliable differential diagnosis must be received in evidence.

This case illustrates the fundamental problem with differential diagnosis . . . . The doctor has not offered any reliable basis for concluding that Rezulin is capable of causing the cirrhosis that

1           As a final matter, Ruggiero--relying on language in  
2   McCullock--argues that any fault in Dr. Dietrich's use of  
3   a differential diagnosis goes to weight, not  
4   admissibility. After the McCullock Court reviewed a  
5   number of factors underlying the opinion of the  
6   plaintiff's expert, the Court stated that "[d]isputes as  
7   to the strength of his credentials, faults in his use of  
8   differential etiology as a methodology, or lack of textual  
9   authority for his opinion, go to the weight, not the  
10   admissibility, of his testimony." Id. at 1044. Ruggiero  
11   is over-reading that passage. The opinion had held,  
12   *supra*, that the district court did not abuse its  
13   discretion in ruling that the expert's opinion in that  
14   case was admissible; in the quoted passage, the Court was  
15   merely signaling that any remaining objection as to the  
16   expert's credentials or methodology was for the  
17   consideration of the jury. In any event, Ruggiero's  
18   reading of McCullock is precluded by the Supreme Court's  
19   subsequent decision in Joiner. In Joiner, the Court held

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caused the liver failure that resulted in Mr.  
Ruggiero's death. In other words, he has offered  
no reliable ground upon which Rezulin may be  
"ruled in" as a plausible cause of the cirrhosis.

1     that "conclusions and methodology are not entirely  
2     distinct from one another," and that "[a] court may  
3     conclude that there is simply too great an analytical gap  
4     between the data and the opinion proffered." 522 U.S. at  
5     146. Following Joiner, we held that "when an expert  
6     opinion is based on data, a methodology, or studies that  
7     are simply inadequate to support the conclusions reached,  
8     Daubert and Rule 702 mandate the exclusion of that  
9     unreliable opinion testimony." Amorgianos v. Nat'l R.R.  
10    Passenger Corp., 303 F.3d 256, 266 (2d Cir. 2002). In  
11    light of Joiner and Amorgianos, Ruggiero's reliance on  
12    McCulloch is unpersuasive.

13  
14                   \* \* \* \*

15           We have considered Ruggiero's remaining arguments and  
16    find each to be without merit. The judgment of the  
17    district court is affirmed.